HHS Public Access

Author manuscript

Fatigue. Author manuscript; available in PMC 2015 July 13.

Published in final edited form as:

Fatigue. 2015 ; 3(3): 142–155. doi:10.1080/21641846.2015.1039289.

Perceived Fatigue Interference and Depressed Mood: Comparison of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis Patients with Fatigued Breast Cancer Survivors

Daniel L. Hall[1], **Michael H. Antoni**[1,2,3], **Emily G. Lattie**[1], **Devika R. Jutagir**[1], **Sara J. Czaja**[3], **Dolores Perdomo**[3], **Suzanne C. Lechner**[2], **Jamie M. Stagl**[4], **Laura C. Bouchard**[1], **Lisa M. Gudenkauf**[1], **Lara Traeger**[4], **MaryAnn Fletcher**[5], and **Nancy G. Klimas**[5]

Daniel L. Hall: dhall@psy.miami.edu; Michael H. Antoni: mantoni@miami.edu; Emily G. Lattie: elattie@psy.miami.edu; Devika R. Jutagir: djutagir@psy.miami.edu; Sara J. Czaja: sczaja@med.miami.edu; Dolores Perdomo: dperdomo@med.miami.edu; Suzanne C. Lechner: slechner@med.miami.edu; Jamie M. Stagl: jstagl@mgh.harvard.edu; Laura C. Bouchard: lbouchard@psy.miami.edu; Lisa M. Gudenkauf: lgudenkauf@psy.miami.edu; Lara Traeger: ltraeger@mgh.harvard.edu; MaryAnn Fletcher: mfletcher@nova.edu; Nancy G. Klimas: nklimas@nova.edu

[1]Department of Psychology, University of Miami

[2]Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine

[3]Department of Psychiatry and Behavioral Sciences, University of Miami

[4]Department of Psychiatry, Massachusetts General Hospital/Harvard Medical School

[5]Institute for Neuro Immune Medicine, Nova Southeastern University

Abstract

Objective—Persistent fatigue and depressive symptoms are both highly prevalent among patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) as well as breast cancer survivors. This study aimed to assess and directly compare perceptions of fatigue as highly interfering in one's daily functioning in both patient populations to better understand their relationships with depressed mood.

Methods—Participants were 95 female CFS/ME patients and 67 females who were approximately 5 years post-treatment for stage 0-III breast cancer presenting with clinically elevated fatigue severity. Self-report measures were obtained on participants' fatigue-related interference in daily functioning and fatigue severity as well as depressed mood. Hierarchical regression was used to test effects controlling for relevant demographic, psychosocial, and medical covariates.

Results—CFS/ME patients endorsed greater depressed mood and fatigue interference than did fatigued breast cancer survivors, *p's*<.001. These factors were significantly positively correlated among CFS/ME patients (β=.36, *p*<.001), but not the fatigued breast cancer survivors (β=.18, *p*=.19).

Conclusions—CFS/ME patients reported elevated fatigue symptoms and depression relative to fatigued breast cancer survivors. In the former group, greater depressed mood was highly and

significantly associated with greater fatigue-related inference in daily activities. Potential targets for cognitive behavioral interventions are discussed.

Keywords

Fatigue; Chronic Fatigue Syndrome; Breast Cancer; Depression

Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is a disorder characterized by severe and debilitating fatigue lasting more than six months with no known cause [1]. Breast cancer survivors also frequently endorse clinically significant levels of fatigue up to five years after treatment [2–7]. Across both conditions, fatigue can impair one's quality of life and may result in functional losses, depressive symptoms, and neuroimmune changes [8–11], which can further exacerbate fatigue. Adults diagnosed with CFS/ME as well as those with different types of cancer rank fatigue as among the most distressing and impairing aspects of their illness [10, 12].

Individuals with CFS/ME and cancer not only report elevated fatigue but show remarkably high rates of co-morbid depression or depressive symptoms, approaching 32% in CFS/ME patients [9, 13] and 15–16% in breast cancer survivors 5 or more years post-treatment [3, 14–17]. Although fatigue may share some characteristics with depression, these symptoms can manifest independent of the other and may have different precipitants [11, 18, 19].

Importantly, a patient's concerns about fatigue and its impact can trigger or worsen emotional distress states. Recent literature suggests that fatigue-related cognitive appraisals play a role in the presentation of comorbid depressive symptoms in medically ill populations [9, 20–25]. For instance, among persons with CFS/ME, cognitions related to fatigue symptom focusing, anticipation of burden, and beliefs about fatigue are considered to contribute to the maintenance of depression symptoms [26, 27]. Cancer survivors may report feelings of disappointment, frustration, and hopelessness when post-treatment fatigue interferes with their occupational and interpersonal functioning [17, 28], which can be exacerbated by specific beliefs about fatigue [29]. Fatigue-related cognitions may be addressed directly with cognitive behavioral therapy (CBT) [22, 30]. However, in terms of CBT, it is unlikely that one size fits all, and it remains unknown whether CFS/ME and cancer survivors differ in their fatigue-related appraisals and whether these appraisals are tied to depressive symptoms in each of these populations. Gaining insight about fatigue appraisals and their relations with depressive symptoms in each of these groups could yield important information for the targeted application of CBT in these populations.

The majority of literature investigating the relations between fatigue appraisals and emotional states has emphasized two components of fatigue: fatigue interference in daily functioning and fatigue severity [31]. Both aspects of fatigue are often measured via self-report questionnaires, prompting the respondent to rate on a Likert-type numerical scale the magnitude of fatigue experienced (severity) or interference of that fatigue in daily activities such as work and social behaviors, during a specific recall period. In other words, fatigue severity reflects how much fatigue one has experienced, and fatigue interference reflects one's perception of the impact fatigue has had on one's own day-to-day functioning. Generally, among medical patients with chronic illness, *fatigue interference in daily*

functioning has been associated with decrements in physical and mental quality of life [31], though the comparative contribution of this fatigue perception to distress states among different fatigued populations has been underexplored. Traeger and colleagues [20] recently determined that, among cancer patients with cancer-related fatigue, clinically elevated depressive symptoms were associated with fatigue interference levels being equal to or greater than fatigue severity levels. The authors noted that, compared with fatigue severity, fatigue interference may be more strongly related to depression among fatigued cancer patients.

To our knowledge, no study has examined these associations among patients with CFS/ME or long-term breast cancer survivors. Comparison studies between fatigued cancer patients and CFS/ME patients indicate that while both groups report similar fatigue severity, CFS/ME patients report greater decrements in physical quality of life, including more functional impairment, less physical activity, and less efficacy about self-management of symptoms [7, 32]. These findings suggest that CFS/ME patients are disadvantaged relative to other fatigued medical patients, which may manifest in relatively greater perceived interference. Furthermore, if depressed mood in CFS/ME patients is shown to be linked with interference from fatigue, clinical researchers and practitioners may target perceived fatigue interference to ameliorate emotional distress among patients.

Researchers have yet to determine the extent to which fatigue interference relates to concurrent depressive symptoms differently in persons with CFS/ME versus breast cancer. Research that can answer such questions directly should include individuals with cancer who have completed primary treatment (i.e., to control for new sources of fatigue) and also experience elevated fatigue levels. Because the modal person with CFS/ME is female [33], we focused our comparison to two samples: women with CFS/ME and fatigued female breast cancer survivors who were in remission and approximately five years post-completion of primary treatment. This time point was selected for breast cancer survivors for three reasons. First, breast cancer survivors at five years post-treatment still frequently endorse high levels of fatigue [2–5]. Second, by the five-year diagnosis mark, sufficient time has likely passed that their experiences of fatigue and/or depression are not secondary to acute psychological or physiological sequelae of diagnosis and treatment [4, 34]. Third, by five years after treatment, breast cancer survivors have dealt with any persisting symptoms chronically, making them a suitable comparison group for patients with the chronic symptoms of CFS/ME.

In this study, we sought to address the gaps in the literature identified above with the following aims and hypotheses. In Aim 1 we assessed and compared fatigue interference among female CFS/ME patients to that of female breast cancer survivors who were five years post-treatment. Based on prior literature, we hypothesized that on average CFS/ME patients' fatigue interference scores would be higher than those of the breast cancer survivors. Aim 2 assessed the relations between fatigue interference and concurrent depressed mood in CFS/ME and breast cancer survivors. We explored whether fatigue interference would be positively related with more depressive symptoms in both patient samples.

Method

Participants

CFS/ME patients and breast cancer survivors were recruited separately for longitudinal studies of stress management and psychosocial processes in these populations. Details of recruitment for these studies have been reported elsewhere [35, 36]. Participants in the present comparison study were women who provided data for these two studies. From the original sample of 117 patients with CFS/ME, we retained data for female participants (n = 95). The breast cancer study sample consisted of 130 women from the parent intervention study who consented to participate in a follow-up study examining five-year survivorship experiences. Baseline fatigue interference, fatigue severity, and depressed mood were similar among follow-up study participants and non-participants. From these two samples, we retained data for women who endorsed clinically elevated levels of fatigue as indicated by a Fatigue Symptom Inventory fatigue severity subscale score of 3 or greater [37]. The final comparison samples consisted of 95 women with CFS/ME and 67 fatigued breast cancer survivors.

Participants from both samples were recruited via physician referral, support groups, special events including conferences. Recruitment of the CFS/ME sample also utilized advertisements on CFS-related websites. The majority of potential participants screened lived in South Florida and were referred by local physicians. CFS/ME participants were required to have a physician-determined CFS diagnosis according to the Centers for Disease Control and Prevention (CDC) criteria [1]. Breast cancer survivors were required to have undergone surgery for non-metastatic stage 0–IIIb breast cancer five years prior to data collection as verified by their clinician. For the present analysis, breast cancer survivors could not be included if a cancer recurrence or prior CFS/ME diagnosis was indicated. Exclusion criteria for both CFS/ME and breast cancer patients included prior cancer (i.e., prior to the breast cancer), prior psychiatric treatment for a serious disorder (e.g., psychosis, suicidality), and lack of fluency in English. Potential participants were also excluded for cognitive impairment, if they met criteria for schizophrenia, bipolar disorder, or substance abuse, or were actively suicidal, or if they had comorbid autoimmune or infectious illness or blood-related disease. The studies that recruited these participants were approved by the local institutional review board. All participants provided written informed consent.

Measures

Demographic and Disease-Related Information—Information about participants' demographics and medical condition was collected via self-report. These variables included age, race/ethnicity, marital status, employment status, education level, number of children, and years since diagnosis. Due to the potential influence of several of these factors on depressive symptoms [38], these variables were included as potential covariates in all analyses. Categorical variables (education, race/ethnicity, marital status, and employment) were dichotomized to indicate whether the participants completed college (yes/no), identified as non-Hispanic White (yes/no), were married or in a committed partnership (yes/no), and employed full-time (yes/no).

Fatigue Interference and Severity—Participants completed the Fatigue Symptom Inventory (FSI), a self-report measure of fatigue that was developed and validated with breast cancer patients [39]. The FSI consists of two subscales, measuring fatigue interference and fatigue severity. The fatigue interference subscale consists of 7 Likert-type items measured on 11-point scales (0=No Interference; 10=Extreme Interference) that assess the degree to which fatigue during the past week was appraised to interfere with "general level of activity", "ability to bathe and dress", "normal work activity (includes both work outside the home and housework)", "ability to concentrate", "relations with other people", and other aspects of life. The fatigue severity subscale consists of 4 items measured on 11-point scales (0=Not at all fatigued; 10=As fatigued as I could be) that assess current fatigue level in addition to most, least, and average fatigue levels during the past week. Item responses for each subscale are averaged to create a subscale score.[1]

In both samples, reliability of interference and severity subscales were observed to be in the acceptable range. Among the CFS/ME patients, interference and severity alphas (αs) were 0.86 and 0.79, respectively. Among the breast cancer survivors, interference and severity αs were 0.93 and 0.77, respectively. In the combined sample, fatigue severity was positively correlated with fatigue interference (r=.76, p<.001).

Depressive Symptoms—Participants completed the Center for Epidemiologic Studies Depression Scale (CES-D) [40]. The CES-D measures depressive symptoms experienced over the past week by asking participants to rate 20 items such as "I felt that I could not shake off the sad feelings even with help" on a 4-point scale, from 0 (rarely or none of the time, <1 day) to 3 (most or all of the time, 5–7 days). Items are then summed to create a total score. A clinical cutoff score of 16 or greater indicates clinically elevated depressive symptomatology. Due to the potential overlap of fatigue-related and depressive symptoms [41], an important methodological consideration was to isolate depressed mood items from those on the CES-D associated with vigor, energy, and concentration-related difficulties, as has been done previously [40, 41]. A depressed mood score was thus calculated by summing a subset of 7 items that describe mood disturbance and not somatic symptoms [41]. Although hypothesis testing utilized depressed mood scores, for descriptive purposes we also include analyses of total CES-D scores. Cronbach αs for CES-D total scores in both samples were acceptable (0.91 in CFS/ME patients and 0.89 in breast cancer survivors) as were CES-D depressed mood scores (0.91 in CFS/ME patients and 0.85 in breast cancer survivors).

Statistical Analyses

Statistical analyses were performed using SPSS version 19.0. All variables were examined for normality within each sample. Demographic and medical variables were analyzed for

[1]The original FSI presents response options on a scale from 0 (not at all fatigued/no interference) to 10 (as fatigued as I could be/extreme interference). The CFS/ME sample was administered the correct range of response options (0 to 10). However, the breast cancer survivors were presented with response options from 1 (not at all fatigued/no interference) to 9 (as fatigued as I could be/extreme interference).
In order to make meaningful comparisons between these samples, we arrived at a method to transform the breast cancer survivor sample's FSI data to convert item scores from a scale of 1 to 9 to the correct scale of 0 to 10 by conducting a linear conversion.

group differences between the CFS/ME and breast cancer samples using an independent-samples t-test and Pearson Chi-Square test.

Analyses of covariance (ANCOVA) compared fatigue interference and, for descriptive purposes, fatigue severity of CFS/ME patients and breast cancer survivors after controlling for relevant covariates. Then, the two samples were compared in terms of level of depressed mood as well as total depressive symptoms. Finally, a series of multiple regression models were used to test whether higher fatigue interference scores were associated with greater depressed mood in either patient group after controlling for covariates.

Results

Demographic and medical information about study participants are summarized in Table 1. All continuous variables were normally distributed within each sample. On average, CFS/ME patients and breast cancer survivors were in their early 50's, had graduated from college, were predominantly non-Hispanic White, and had given birth to at least one child. Compared with the CFS/ME sample, the breast cancer survivors were 4 years older, married or partnered, and employed full time. Additionally, CFS/ME patients reported having a slightly longer duration since diagnosis than the breast cancer patients.

As depicted in Table 2, self-reported overall depressive symptoms were greater in the CFS/ME sample than the breast cancer sample [CES-D total score, $t(160)=7.62$, $p<.001$], as were scores of depressed mood [CES-D depressed mood, $t(160)=7.62$, $p<.001$]. Among CFS/ME patients, 72 (76%) reported clinically meaningful levels of depression. In contrast, significantly fewer breast cancer survivors reported clinically meaningful depression (n=17, 25%, $X^2(1)=40.34$, $p<.001$).

Aim 1

Our first aim was to compare fatigue interference scores among CFS/ME and breast cancer survivors. We tested an ANCOVA model controlling for age, race/ethnicity, education level, marital status, employment status, number of children, and time since diagnosis. Actual means are reported. Results indicated that CFS/ME patients (M=7.03, SD=1.90) had significantly higher fatigue interference scores than did breast cancer survivors (M=2.62, SD=2.11), $F(1,150)=115.36$, $p<.001$. The partial η^2 was .44, indicating a moderate effect size. For descriptive purposes, we tested another ANCOVA modeling similarly structured but predicting fatigue severity scores. CFS/ME patients (M=6.83, SD=1.35) had significantly higher fatigue severity scores compared with breast cancer survivors (M=4.65, SD=1.53), $F(1,150)=40.08$, $p<.001$, partial $\eta^2=.21$ (modest effect).

Aim 2

To address the question of whether depressed mood could be attributable to group differences pertaining to fatigue interference, hierarchical regression models were tested including a group-by-fatigue variable interaction term. Step 1 included covariates, Step 2 patient group and the mean-centered fatigue interference score, and Step 3 a patient group-by-fatigue interference interaction term. The model was tested to predict CES-D depressed mood scores. Results of this analysis yielded a borderline significant interaction ($p=.058$) for

the group-by-fatigue interference term. Follow-up analyses of simple effects within each patient group controlling for covariates indicated that CFS/ME patients' fatigue interference scores were significantly associated with greater depressed mood (β=.36, $p<.001$), while this relationship was not significant among breast cancer survivors (β=.18, $p=.19$). For descriptive purposes, models were also tested with fatigue severity as predictor, and with CES-D total scores as the outcome; however, no significant group-by-fatigue interactions were indicated, *ps*>.58.

Discussion

This study compared the experiences of daily fatigue in two fatigued patient samples: women with CFS/ME and women who had completed breast cancer treatment five years prior and endorsed experiencing clinically elevated fatigue. Specifically, we examined the phenomenon of fatigue interference in activities of daily living and its relationships with depressed mood in these two medical groups.

The majority (> 70%) of CFS/ME patients in this study reported clinically elevated levels of depressive symptoms, which is greater than rates of depression in CFS/ME reported elsewhere [9]. Among breast cancer survivors, rates of clinically elevated depressive symptoms (25%) were also higher than reports in the literature for cancer survivors [20, 42]. The elevated presence of depressive symptoms could be due to several factors. All women in this study had enrolled in clinical trials testing a stress management intervention, and may have been experiencing at least some depressive symptoms, prompting them to enroll. Furthermore, methodological issues regarding the measurement of depressive symptoms in CFS/ME patients and other fatigued medical populations have been well documented, as several CFS/ME and fatigue-related symptoms overlap with criteria for major depression (e.g., psychomotor retardation, cognitive difficulties, and decreased energy levels).

While these symptoms may share similar physiological underpinnings [18], it is thought that depressive symptoms and fatigue severity may function independently in CFS/ME patients and breast cancer survivors [19, 43]. Still, we recognize that the endorsement of fatigue-related symptoms on the CES-D could have resulted in some participants' total scores rising above the suggested clinical cutoff score of 16. Given the potential confound of counting fatigue-related items on our measure of depression, we analyzed group differences between our two samples focusing on depressed mood. The examination of mood disturbance as a correlate to fatigue interference is a methodological strength, and builds on recent findings from Bennett and colleagues [6] showing that mood disturbance and fatigue-related difficulties among breast cancer survivors, patients with CFS/ME, and patients with major depression are orthogonal, or statistically independent.

Participants from both populations were only included if they endorsed clinically elevated levels of fatigue using criteria established by Donovan et al. [37]. Although all women were fatigued, the CFS/ME sample endorsed higher levels of fatigue severity and greater decrements in functioning due to fatigue (i.e., decrements in their social, occupational, and instrumental activities of daily living attributed to fatigue) than did breast cancer survivors. As data were obtained from participants enrolled in larger longitudinal studies, these results

may not typify the experiences of all CFS/ME patients and breast cancer survivors. Still, our findings are consistent with previous comparisons of fatigue experiences between these two populations [7].

The finding that CFS/ME patients had greater fatigue interference compared to fatigued breast cancer survivors may be due to several factors. Though both populations endorsed experiencing persistent fatigue, it may be that components of the fatigue are qualitatively distinct in these populations. In a comparison study, Servaes and colleagues [44] found that CFS/ME patients reported relatively greater difficulties with concentration than did severely fatigued disease-free cancer patients, though these samples endorsed similar difficulties with motivation and physical activity. It may be plausible that this neurocognitive component of fatigue results in greater fatigue interference for CFS/ME patients versus fatigued cancer survivors. However, Bennet and colleagues' [32] qualitative study examining fatigue experiences among women with CFS/ME or cancer-related fatigue found that both groups experience similar cognitive difficulties. Both groups also endorsed concerns with fatigue (e.g., "tiredness", "lack of energy") and mood disturbance (e.g., "low mood", "frustration"). Thus, whether differences in fatigue interference between these patient groups are due to differences in cognitive difficulties, or "mental fatigue", warrants further investigation.

Fatigue Impact and Cognitive Problems

To attempt to address the relation of fatigue interference and cognitive difficulties, we conducted exploratory analyses examining group differences an FSI item assessing the impact of fatigue on one's "ability to concentrate". A hierarchical regression to predict scores on this item found CFS/ME patients to have significantly higher scores than did breast cancer survivors ($p<.001$). However, there was no significant group-by-item interaction when predicting depressed mood scores. Thus while women with CFS/ME tend to endorse greater cognitive impairment from fatigue than breast cancer survivors, this difference seemed not to fully explain group differences in depressed mood.

We also explored whether group differences existed on an item assessing the impact of fatigue on one's "mood", and if an observed difference accounted for group differences in depressed mood. An exploratory ANCOVA predicting scores on this item revealed that CFS/ME patients had significantly higher scores on this item than did breast cancer survivors ($p<.001$). Additionally, the perceived impact of fatigue on mood was significantly associated with greater depressed mood among CFS/ME patients ($p<.001$), but not breast cancer survivors. These data suggest that CFS/ME patients endorse higher fatigue impacts on their mood which may actually lead to a more depressed mood. Interestingly, this was not true of our breast cancer survivor sample.

These exploratory results provide insight into results from Aim 2, which revealed a near-significant group-by-fatigue interference interaction when predicting levels of depressed mood. Fatigue interference was significantly positively related to depressed mood among CFS/ME patients, but not among breast cancer survivors. The emotional impact of feeling limited by one's fatigue therefore appears to be more salient among the CFS/ME patients, for whom there was a positive correlation of moderate effect size between fatigue interference and depressed mood. Moreover, our exploratory analyses suggest that this link

is not due to group differences in ability to concentrate, but rather the mood-related decrements that CFS/ME patients identify as resulting from fatigue.

Fatigue, mood and psychosocial factors

Why might CFS/ME patients but not necessarily breast cancer survivors attribute impairments in mood to fatigue? Compared to severely fatigued disease-free breast cancer patients, Servaes and colleagues [7] found that CFS/ME patients report having less self-efficacy with regard to self-management of fatigue and resultantly more mood disruption. Indeed, CFS/ME patients tend to perceive they have a paucity of adequate support [45]. Compared with CFS/ME, breast cancer has a higher prevalence, and, arguably, greater media presence, research funding, and medical knowledgebase, so it is plausible that CFS/ME patients perceive relatively fewer resources available for managing their symptoms. Future research could investigate whether social support mediates the influence of perceived fatigue interference on depressive symptoms within this population.

Another potential explanation is that fatigue represents a core feature of the “illness experience” for CFS/ME patients, to which patients may readily attribute emotional sequelae. Depressed mood, cognitive disturbance, and other health impairments in CFS/ME may be perceived as secondary to the core feature of CFS/ME diagnosis: persistent fatigue [32, 45]. Alternatively, fatigued breast cancer survivors may attribute low mood to cancer diagnosis, treatment, or long-term physical or psychosocial changes since having cancer [15, 16]. That is, mood disturbance among these women may be more closely related to factors other than their fatigue, such as body image, relationship satisfaction, health-related quality of life, and prior episodes of depression [16, 46].

We suggest that healthcare providers of both populations monitor psychosocial adjustment to fatigue as well as depressed mood. In particular, clinicians treating patients with CFS/ME should assess for depressed mood when high fatigue interference is indicated. We further suggest that interventions aiming to ameliorate mood disturbance in patients with CFS/ME may be strengthened by helping patients get psychosocial needs met when faced with persistent fatigue, and by managing unhelpful beliefs about fatigue that could exacerbate emotional distress.

Limitations

This study had several important limitations. We compared two fatigued medical groups, and our findings may not generalize to other fatigued populations. As many other medical populations are known to struggle with fatigue (e.g., patients with multiple sclerosis, autoimmune and inflammatory illness, and spinal cord injury), future research with these patients may consider examining both fatigue severity and fatigue interference. Furthermore, there was a high prevalence of college-educated women among our sample of breast cancer survivors, which may not reflect the general population. Although breast cancer survivorship has a small, positive correlation with education level [47], there may also have been a selection bias of breast cancer survivors with higher education within the present sample.

Future studies would benefit from recruiting women with a broader range of formal education backgrounds. Additionally, all measures were obtained via self-report.

Supplementary measures of fatigue, such as actigraphy or physiological exertion tasks, could yield more objective information about participants' energy levels. Relatedly, depressive symptoms could have been measured using a structured clinical interview by a trained clinician. Given the relative ease of administering the FSI, we agree with prior reports [20] that clinics seeking a preliminary screening tool in populations dealing with chronic fatigue may benefit from using this measure. Similarly, clinicians can ask their patients about the impact of fatigue on their daily functioning, as this information may indicate whether the patient could benefit from subsequent screening for depression.

Conclusions

Taken together, findings from this study indicate that the CFS/ME patients may experience elevated fatigue interference relative to fatigued breast cancer survivors. In CFS/ME patients, fatigue interference was most closely associated with concurrent depressive symptoms, whereas this association was attenuated and non-significant in breast cancer survivors. Interventions that target perceptions of fatigue interference in CFS/ME could potentially reduce depressed mood, though this remains untested. In particular, cognitive-behavioral treatments may be especially helpful in restructuring maladaptive fatigue appraisals, making fatigue more manageable [22, 48–51]. These interventions have been efficacious in improving patients' emotional and neuroimmune profiles, leading to improved physical health outcomes [24, 52–57]. Targeting these forms of intervention to persons with CFS/ME who present with elevated fatigue interference should be an important area of future clinical research.

Acknowledgments

None.

Abbreviations used

CFS/ME	Chronic Fatigue Syndrome/Myalgic Encephalomyelitis
CBT	cognitive behavioral therapy
CDC	Centers for Disease Control and Prevention
FSI	Fatigue Symptom Inventory
CES-D	Center for Epidemiologic Studies Depression Scale
HPA	hypothalamic-pituitary-adrenal

References

1. Fukuda K, et al. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Annals of Internal Medicine. 1994; 121(12):953–959. [PubMed: 7978722]
2. Hall DL, Mishel MH, Germino BB. Living with cancer-related uncertainty: associations with fatigue, insomnia, and affect in younger breast cancer survivors. Supportive Care in Cancer. 2014:1–7.
3. Bower JE, et al. Fatigue in Breast Cancer Survivors: Occurrence, Correlates, and Impact on Quality of Life. Journal of Clinical Oncology. 2000; 18(4):743–753. [PubMed: 10673515]

4. Von Ah DM, Kang DH, Carpenter JS. Predictors of cancer-related fatigue in women with breast cancer before, during, and after adjuvant therapy. Cancer Nursing. 2008; 31(2):134–144. [PubMed: 18490890]
5. Stasi R, et al. Cancer-related fatigue. Cancer. 2003; 98(9):1786–1801. [PubMed: 14584059]
6. Bennett BK, et al. Characterization of Fatigue States in Medicine and Psychiatry by Structured Interview. Psychosomatic medicine. 2014; 76:379–388. [PubMed: 25076512]
7. Servaes P, et al. Fatigue after breast cancer and in chronic fatigue syndrome: Similarities and differences. Journal of Psychosomatic Research. 2002; 52(6):453–459. [PubMed: 12069869]
8. Bower JE, et al. Fatigue and proinflammatory cytokine activity in breast cancer survivors. Psychosomatic Medicine. 2002; 64(4):604–611. [PubMed: 12140350]
9. Cella M, et al. Cognitions, behaviours and co-morbid psychiatric diagnoses in patients with chronic fatigue syndrome. Psychological medicine. 2013; 43(02):375–380. [PubMed: 22571806]
10. Antoni MH, et al. Psychosocial correlates of illness burden in chronic fatigue syndrome. Clinical Infectious Diseases. 1994; 18(Supplement 1):S73–S78. [PubMed: 8148457]
11. Bower JE. Cancer-related fatigue: Mechanisms, risk factors, and treatments. Nature Reviews Clinical Oncology. 2014; 11(10):597–609.
12. Hwang SS, et al. Multidimensional independent predictors of cancer-related fatigue. Journal of pain and symptom management. 2003; 26(1):604–614. [PubMed: 12850643]
13. Reeves WC, et al. Prevalence of chronic fatigue syndrome in metropolitan, urban, and rural Georgia. Popul Health Metr. 2007; 5(5):1–10. [PubMed: 17288607]
14. Ng CG, et al. The prevalence and pharmacotherapy of depression in cancer patients. Journal of affective disorders. 2011; 131(1):1–7. [PubMed: 20732716]
15. Reyes-Gibby CC, et al. Depressive symptoms and health-related quality of life in breast cancer survivors. Journal of Women's Health. 2012; 21(3):311–318.
16. Burgess C, et al. Depression and anxiety in women with early breast cancer: five year observational cohort study. Bmj. 2005; 330(7493):702–705. [PubMed: 15695497]
17. Banthia R, et al. Fatigued breast cancer survivors: the role of sleep quality, depressed mood, stage and age. Psychology and Health. 2009; 24(8):965–980. [PubMed: 20205039]
18. Anderson G, Berk M, Maes M. Biological phenotypes underpin the physio-somatic symptoms of somatization, depression, and chronic fatigue syndrome. Acta Psychiatrica Scandinavica. 2014; 129(2):83–97. [PubMed: 23952563]
19. Ho SY, et al. A Longitudinal Study of Depression, Fatigue, and Sleep Disturbances as a Symptom Cluster in Women with Breast Cancer. Journal of Pain and Symptom Management. In Press.
20. Traeger L, et al. Parsing depression from fatigue in patients with cancer using the fatigue symptom inventory. Journal of pain and symptom management. 2011; 42(1):52–59. [PubMed: 21398085]
21. Price JR, et al. Cognitive behaviour therapy for chronic fatigue syndrome in adults. Cochrane Database Syst Rev. 2008; 3
22. White P, et al. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. The Lancet. 2011; 377(9768):823–836.
23. Petrie K, Moss-Morris R, Weinman J. The impact of catastrophic beliefs on functioning in chronic fatigue syndrome. Journal of Psychosomatic Research. 1995; 39(1):31–37. [PubMed: 7760301]
24. Stahl D, Rimes K, Chalder T. Mechanisms of change underlying the efficacy of cognitive behaviour therapy for chronic fatigue syndrome in a specialist clinic: a mediation analysis. Psychological medicine. 2013:1–14.
25. Friedberg F, Krupp LB. A comparison of cognitive behavioral treatment for chronic fatigue syndrome and primary depression. Clinical Infectious Diseases. 1994; 18(Supplement 1):S105–S110. [PubMed: 8148435]
26. Knoop H, et al. The central role of cognitive processes in the perpetuation of chronic fatigue syndrome. Journal of Psychosomatic Research. 2010; 68(5):489–494. [PubMed: 20403509]
27. Wiborg JF, et al. Does a decrease in avoidance behavior and focusing on fatigue mediate the effect of cognitive behavior therapy for chronic fatigue syndrome? Journal of Psychosomatic Research. 2011; 70(4):306–310. [PubMed: 21414449]

28. Meeske K, et al. Fatigue in breast cancer survivors two to five years post diagnosis: a HEAL Study report. Quality of Life Research. 2007; 16(6):947–960. [PubMed: 17457697]
29. Jacobsen PB, Andrykowski MA, Thors CL. Relationship of catastrophizing to fatigue among women receiving treatment for breast cancer. Journal of Consulting and Clinical Psychology. 2004; 72(2):355–361. [PubMed: 15065968]
30. Gielissen MF, et al. Effects of cognitive behavior therapy in severely fatigued disease-free cancer patients compared with patients waiting for cognitive behavior therapy: a randomized controlled trial. Journal of Clinical Oncology. 2006; 24(30):4882–4887. [PubMed: 17050873]
31. Whitehead L. The measurement of fatigue in chronic illness: a systematic review of unidimensional and multidimensional fatigue measures. Journal of pain and symptom management. 2009; 37(1):107–128. [PubMed: 19111779]
32. Bennett B, et al. The experience of cancer-related fatigue and chronic fatigue syndrome: a qualitative and comparative study. Journal of Pain and Symptom Management. 2007; 34(2):126–135. [PubMed: 17544246]
33. Nacul LC, et al. Prevalence of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in three regions of England: a repeated cross-sectional study in primary care. BMC medicine. 2011; 9(1):91. [PubMed: 21794183]
34. Bower JE. Fatigue in Cancer Patients and Survivors: Mechanisms and Treatment. Primary Psychiatry. 2005; 12(5):53–57.
35. Lattie EG, et al. Stress management skills, neuroimmune processes and fatigue levels in persons with chronic fatigue syndrome. Brain, Behavior, and Immunity. 2012; 26(6):849–858.
36. Stagl JM, et al. Randomized Controlled Trial of Cognitive Behavioral Stress Management in Breast Cancer: A Brief Report of Effects on 5-Year Depressive Symptoms. 2014
37. Donovan KA, et al. Identifying clinically meaningful fatigue with the Fatigue Symptom Inventory. Journal of pain and symptom management. 2008; 36(5):480–487. [PubMed: 18495413]
38. Blazer DG, Kessler RC. The prevalence and distribution of major depression in a national community sample: the National Comorbidity Survey. American Journal of Psychiatry. 1994; 151(7):979–986. [PubMed: 8010383]
39. Hann D, et al. Measurement of fatigue in cancer patients: development and validation of the Fatigue Symptom Inventory. Quality of Life Research. 1998; 7(4):301–310. [PubMed: 9610214]
40. Radloff LS. The CES-D scale a self-report depression scale for research in the general population. Applied psychological measurement. 1977; 1(3):385–401.
41. Hertzog C, et al. Measurement properties of the Center for Epidemiological Studies Depression Scale (CES-D) in older populations. Psychological Assessment: A Journal of Consulting and Clinical Psychology. 1990; 2(1):64.
42. Mast ME. Survivors of breast cancer: illness uncertainty, positive reappraisal, and emotional distress. Oncology Nursing Forum. 1998; 25(3):555–562. [PubMed: 9568610]
43. Valero S, et al. The role of neuroticism, perfectionism and depression in chronic fatigue syndrome. A structural equation modeling approach. Comprehensive psychiatry. 2013; 54(7):1061–1067. [PubMed: 23759150]
44. Servaes P, et al. Fatigue in disease-free cancer patients compared with fatigue in patients with chronic fatigue syndrome. Supportive care in cancer. 2001; 9(1):11–17. [PubMed: 11147137]
45. Schoofs N, et al. Death of a lifestyle: the effects of social support and healthcare support on the quality of life of persons with fibromyalgia and/or chronic fatigue syndrome. Orthopaedic Nursing. 2004; 23(6):364–374. [PubMed: 15682879]
46. Kim SH, et al. Fatigue and Depression in Disease-Free Breast Cancer Survivors: Prevalence, Correlates, and Association with Quality of Life. Journal of Pain and Symptom Management. 2008; 35(6):644–655. [PubMed: 18358687]
47. Sprague BL, et al. Socioeconomic status and survival after an invasive breast cancer diagnosis. Cancer. 2011; 117(7):1542–1551. [PubMed: 21425155]
48. Lopez C, et al. A pilot study of cognitive behavioral stress management effects on stress, quality of life, and symptoms in persons with chronic fatigue syndrome. Journal of Psychosomatic Research. 2011; 70(4):328–334. [PubMed: 21414452]

49. Castell BD, Kazantzis N, Moss-Morris RE. Cognitive Behavioral Therapy and Graded Exercise for Chronic Fatigue Syndrome: A Meta-Analysis. Clinical Psychology: Science and Practice. 2011; 18(4):311–324.
50. Antoni MH, et al. Cognitive-behavioral stress management intervention decreases the prevalence of depression and enhances benefit finding among women under treatment for early-stage breast cancer. Health Psychology. 2001; 20(1):20–32. [PubMed: 11199062]
51. Vargas S, et al. Sleep Quality and Fatigue after a Stress Management Intervention for Women with Early-Stage Breast Cancer in Southern Florida. International Journal of Behavioral Medicine. 2013:1–11. [PubMed: 21960258]
52. Roberts ADL, et al. Salivary cortisol output before and after cognitive behavioural therapy for chronic fatigue syndrome. Journal of Affective Disorders. 2009; 115(1):280–286. [PubMed: 18937978]
53. Heins MJ, et al. The process of cognitive behaviour therapy for chronic fatigue syndrome: Which changes in perpetuating cognitions and behaviour are related to a reduction in fatigue? Journal of psychosomatic research. 2013; 75(3):235–241. [PubMed: 23972412]
54. Bower JE, Lamkin DM. Inflammation and cancer-related fatigue: Mechanisms, contributing factors, and treatment implications. Brain, Behavior, and Immunity. 2013; 30:S48–S57.
55. McGregor BA, et al. Cognitive–behavioral stress management increases benefit finding and immune function among women with early-stage breast cancer. Journal of Psychosomatic Research. 2004; 56(1):1–8. [PubMed: 14987957]
56. Phillips KM, et al. Stress management intervention reduces serum cortisol and increases relaxation during treatment for nonmetastatic breast cancer. Psychosomatic Medicine. 2008; 70(9):1044–1049. [PubMed: 18842742]
57. Cruess DG, et al. Cognitive-behavioral stress management reduces serum cortisol by enhancing benefit finding among women being treated for early stage breast cancer. Psychosomatic Medicine. 2000; 62(3):304–308. [PubMed: 10845343]

Table 1

Summary of Demographic and Medical Variables

Participant Characteristics	CFS/ME (n = 95)	Breast Cancer (n = 67)	*p*
Age in years, M (SD)	51.31 (11.03)	55.39 (8.48)	<.01
Completed college, *n* (%)	42 (44%)	54 (81%)	<.01
White non-Hispanic, *n* (%)	73 (77%)	48 (72%)	.45
Married/Partnered, *n* (%)	41 (43%)	41 (61%)	.02
Employed full-time, *n* (%)	17 (18%)	46 (69%)	<.001
Number of children, M (SD)	1.07 (1.24)	1.48 (1.13)	.04
Years since diagnosis, M (SD)	7.23 (6.59)	5.22 (0.12)	.01

Note: M=Mean. SD=Standard Deviation. Group differences on continuous variables determined by independent-samples t-test. Group differences on dichotomous variables determined by Pearson Chi-Square test.

Table 2

Summary of Fatigue and Depression-Related Variables

Variable	CFS/ME (n = 95)	Breast Cancer (n = 67)	*p*
Fatigue			
Interference, M (SD)	7.03 (1.90)	2.62 (2.11)	<.001
Severity, M (SD)	6.83 (1.33)	4.65 (1.53)	<.001
Depressive symptoms			
Depressed mood, M (SD)	7.62 (6.27)	3.42 (3.55)	<.001
Continuous, M (SD)	25.70 (12.55)	12.59 (9.27)	<.001
Clinically elevated, *n* (%)	72 (76%)	17 (25%)	<.001

Note: M=Mean. SD=Standard Deviation. Fatigue Interference and Severity from Fatigue Symptom Inventory (FSI) subscales; Depressive symptoms from Center for Epidemiological Studies – Depression (CES-D) measure; Clinically elevated Depressive symptoms defined as a total score of ≥ 16. Group differences on continuous variables determined by independent-samples t-test. Group differences on dichotomous variables determined by Pearson Chi-Square test.